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Effect of perindopril/indapamide/amlodipine fixed-dose combination on peripheral and central hemodynamics and vascular wall stiffness parameters in patients with uncontrolled hypertension

T.A. Netchessova, S.V. Charnyak, L.V. Yakubova. *Republican Scientific Practical Center Cardiology, Laboratory of Hypertension, Minsk, Belarus*

Objective: To evaluate the effects of perindopril/indapamide/amlodipine fixed-dose combination (FDC) on peripheral and central blood pressure (BP) parameters: systolic and diastolic blood pressure (SBP, DBP), central systolic blood pressure (CSBP), central pulse blood pressure (CPBP), augmentation index (AI), and pulse wave velocity (PWV) in patients with uncontrolled arterial hypertension (AH).

Scope and methods of study. FDC was administered to 796 patients with Stage 1-3 AH. Mean age was 57.1 ± 10.5 years; 51% of patients were male, 49% were female. Parameters, such as CSBP, CPBP, AI, PWV and vascular age, were evaluated using an applanation tonometer (SphygmoCor system, Australia) at baseline and after 5 months of treatment.

Results: As a result of FDC administration and dynamic monitoring for 5 months, SBP and DBP levels decreased from $166.5 \pm 15.4/97.4 \pm 8.5$ mm Hg to $130.3 \pm 9.2/80.3 \pm 4.5$ mm Hg ($p < 0.001$). Target levels of SBP and DBP were achieved in 84.6% and 88.2% of all patients, respectively. Target levels were achieved in 100% of patients with Stage 1 AH, in 90% of patients with Stage 2 AH, and in 72% of patients with Stage 3 AH. CSBP levels decreased from 141.7 ± 2.27 to 117.0 ± 2.27 mm Hg ($p < 0.001$), CPBP levels decreased from 51.2 ± 1.9 to 39.4 ± 1.8 mm Hg ($p < 0.001$), AI decreased from 27.4 ± 2.21 to $23.1 \pm 1.71\%$ ($p < 0.05$), and PWV decreased from 10.3 to 7.1 m/sec ($p < 0.05$). Target levels of CSBP and CPBP were achieved in 86.7% and 90% of all patients, respectively. Baseline vascular age was 62.3 ± 2.7 years and showed a statistically significant decrease to 54.8 ± 2.8 years after 5 months ($p < 0.05$).

Conclusion: Triple fixed-dose combination allows to achieve adequate control of BP in the majority of patients with uncontrolled AH, provides statistically significant decrease of peripheral and central BP, has an effect on rigidity and elastic properties of the arterial wall, and leads to a decreased risk of cardiovascular complications.

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CHINA Study of valsartan/amlodipine fixed-dose combination-bAseD long-Term blood pressUre management in HypertenSive Patients: a one-year registry (CHINA STATUS III)

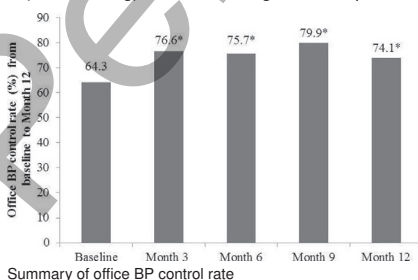
Y. Huo¹, B.W. Zhang¹, Z. Du². ¹Peking University First Hospital, Cardiology, Beijing, China People's Republic of; ²Novartis Pharmaceuticals (China), Shanghai, China People's Republic of. On behalf of CHINA STATUS III study group

Background: In China, hypertension is identified as the second leading risk factor for cardiovascular (CV) diseases. Compared with monotherapy, fixed-dose combination (FDC) antihypertensive therapy has been proposed to offer improved efficacy and enhanced patient compliance. Nevertheless, data on the long-term efficacy and safety of FDC from real-world settings in China is limited.

Purpose: The present observational study evaluated long-term management of hypertension in patients receiving treatment with valsartan/amlodipine fixed-dose combination (Val/Aml FDC) in real-world setting in China.

Methods: This was a prospective, observational, multicenter, real-world registry study wherein patients with hypertension who had already received Val/Aml FDC for at least 4 weeks before study enrollment were observed for 1 year. Investigators recorded patient data every 3 months and for 5 times during the 1-year follow-up period. Effectiveness was assessed as blood pressure (BP) control rate (Office BP control was defined as average BP $< 140/90$ mmHg and $< 135/85$ mmHg for Home BP) and average duration on treatment at the end of study. Safety was monitored by incidence of adverse events (AEs) and serious adverse events (SAEs).

Results: Overall, 985 patients were enrolled (mean \pm SD age: 60.3 ± 11.5 years); of these, 894 were included in the full analysis set who had at least one post-baseline visit, 758 completed the study. At baseline, BP was controlled ($< 140/90$ mmHg) in 64.3% of patients on Val/Aml FDC for at least 4 weeks before enrollment. Office BP control rates improved significantly ($P < 0.0001$) from baseline at months 3, 6, 9, and 12 visits (Figure). Significant reductions in SBP ($P < 0.0001$) were assessed from baseline at months 3 (3.15 mmHg), 6 (3.0 mmHg), and 9 (4.43 mmHg). In addition, significant improvements were observed in home



blood pressure control rate from baseline to months 3 (73.1%), 6 (74.7%), and 9 (77.3%). Adherence to treatment was high: 91% of patients at month 6 reported that they never missed one dose, and 93.4% of patients at month 6 and 95.3% of patients at study end (month 12) maintained their Val/Aml FDC treatment. AEs were reported in 23.3% of patients. A majority of AEs was mild to moderate and 0.6% of patients discontinued Val/Aml FDC because of SAEs.

Conclusion: Val/Aml FDC provided long-term sustained BP control with good tolerability and good long-term compliance in this 1-year, real-world registry study in patients with hypertension from China.

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Ramipril significantly attenuates the development of non-alcoholic steatohepatitis in hyperlipidaemic rabbits

M.C. Soares Sturzeneker, D. Bertolim Precoma, L. Noronha, M. Olandoski, L. Uhlmann Wendling, G.E. Jacomet, A. Gama Palone. *Pontifical Catholic University of Parana, Center of Health and Biological Sciences, Curitiba, Brazil*

Background/Introduction: Non-alcoholic fatty liver disease (NAFLD) is considered as the most frequent cause of chronic hepatic disease in adults. The renin-angiotensin system has been correlated to the whole basic physiopathogenic mechanism of NAFLD in experimental models. Systemic arterial hypertension has been suggested to be associated with NAFLD in approximately 40% of the cases, and NAFLD has been independently associated with an increased risk of arterial hypertension in observational studies. Therefore, we can infer that treating arterial hypertension in NAFLD carriers will be often necessary and that the potential beneficial effects of the antihypertensive might, in this context, influence the choice of the respective drug.

Purpose: Based on these findings, we conducted this study to evaluate the effects of the angiotensin-converting enzyme inhibitor ramipril, used preventively, in NAFLD induced in rabbits fed hyperlipidaemic diet.

Methods: Twenty-nine rabbits were divided into three groups (normal, placebo, and ramipril). The placebo and ramipril groups were fed a ration containing 0.925% cholesterol. The groups were orally administered 0.35 mg/kg/day of ramipril, and an equivalent volume of vehicle was administered to the placebo group. At the end of the 8th week, all rabbits underwent segmental hepatic resection and were euthanized. Blood samples were collected to determine glucose, insulin, creatinine, total cholesterol, triglycerides, high-density lipoprotein cholesterol, and aminotransferase levels at baseline and euthanasia. Haematoxylin and eosin and Gomori trichrome-stained slides were analysed based on the histological scoring system for NAFLD. Sudan III-stained slides were analysed by morphometry and inducible nitric oxide synthase (iNOS) immunostained based on Allred scoring system.

Results: When compared with placebo, ramipril significantly diminished the development of steatosis ($p = 0.032$), lobular inflammation ($p = 0.006$), hepatocellular ballooning ($p = 0.023$), and fibrosis ($p = 0.02$). Based on NAFLD activity score, ramipril significantly reduced the development of non-alcoholic steatohepatitis ($p = 0.003$). The mean area of positivity estimated by morphometry of Sudan III-stained slides in the placebo group was significantly higher compared with ramipril ($p = 0.049$). The expression of iNOS in the placebo group was significantly higher compared with ramipril ($p < 0.001$).

Conclusion(s): The preventive use of ramipril in rabbits fed hyperlipidaemic diet attenuates the development of the whole NAFLD histopathological spectrum. Further studies are required to consolidate the criteria to choose the most appropriate drugs or therapeutic classes for the treatment of arterial hypertension in NAFLD carriers.

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Effect of nebivolol on lipid and metabolic profiles in Korean patients with hypertension: Result from BENEFIT-KOREA study

S.W. Kwon¹, J.-Y. Do², G.-R. Hong³, B.-K. Kim³, W.M. Hwang⁴, S.-H. Kim⁵, J.-Y. Lee⁶, S.W. Park⁷, D.-H. Kim¹. ¹Inha University Hospital, Cardiology, Incheon, Korea Republic of; ²Yeungnam University Medical Center, Cardiology, Gyeongsan, Korea Republic of; ³Yonsei Cardiovascular Center, Cardiology, Seoul, Korea Republic of; ⁴Konyang University Hospital, Nephrology, Daejeon, Korea Republic of; ⁵Boramae Hospital, Cardiology, Seoul, Korea Republic of; ⁶Kangbuk Samsung Hospital, Cardiology, Seoul, Korea Republic of; ⁷A.Menarini Korea Ltd., Seoul, Korea Republic of. On behalf of BENEFIT-KOREA

Background: Unlike conventional beta blockers, several studies proposed the beneficial effect of nebivolol on lipid and metabolic profiles. However, there is no data so far demonstrating the impact of this new generation beta blocker on lipid and metabolic profiles especially in Asian population.

Method: From 3011 enrolled patients in BENEFIT-KOREA study (BENEFITS after 24 weeks of NEBivolol administration For essential hypertension patients with various co-morbidities and treatment environments in KOREA), 754 patients who undergone blood sampling during the study period were investigated. Baseline lipid and metabolic parameters were compared to 12 week and/or 24 week parameters. Patients who had altered lipid lowering medication during the study period were excluded from the analysis.

Result: Mean age of the cohort was 63.5 ± 12.9 years old with male predomi-